1. A method of regulating endothelial cell growth, comprising the step of contacting endothelial cells with a composition comprising a purified polypeptide in an amount effective to regulate endothelial cell growth, wherein said polypeptide:

(a) binds the extracellular domain of Flt4 receptor tyrosine kinase and stimulates Flt4 autophosphorylation;

(b) has an apparent molecular weight of about 23 kD as assessed by SDS-PAGE under reducing conditions; and

(c) has an amino acid sequence comprising a portion of SEQ ID NO: 8 effective to permit binding to the Flt4 extracellular domain.

2. A method according to claim 1, wherein amino terminal amino acids 2 through 18 of said polypeptide have an amino acid sequence corresponding to amino acids 2 through 18 set forth in SEQ ID NO: 5.

3. A method according to claim 1, wherein said polypeptide is purifyable from conditioned media from a PC-3 prostatic adenocarcinoma cell line, said cell line having ATCC CRL No. 1435, using an affinity purification procedure wherein the affinity purification matrix comprises a polypeptide comprising the extracellular domain of Flt4 receptor tyrosine kinase.

4. A method according to claim 1 wherein the endothelial cells are lymphatic endothelial cells.

5. A method of modulating the activity of Flt4 receptor tyrosine kinase (Flt4), comprising the steps of:

identifying a patient in need of modulation of Flt4 activity; and

administering to the patient a composition comprising a purified polypeptide in an amount effective to modulate the activity of Flt4, wherein the polypeptide is selected from the group consisting of:

(a) a polypeptide that binds the extracellular domain (EC) of Flt4, said polypeptide comprising an amino acid sequence comprising a portion of SEQ ID NO: 8 effective to permit such binding; and

(b) an antibody which is specifically reactive with the polypeptide of (a).

6. A method according to claim 5, wherein the composition comprises a polypeptide that binds the extracellular domain of Flt4, said polypeptide comprising a portion of SEQ ID NO: 8 effective to permit such binding.

7. A method according to claim 5, wherein the composition further comprises a pharmaceutically-acceptable diluent, adjuvant, or carrier.

8. A method according to claim 5, wherein the identifying step comprises identifying a patient suffering from a disorder of the lymphatic system, and wherein the polypeptide is administered in an amount effective to modulate Flt4 activity in endothelial cells of lymphatic vessels of the patient.

9. A method according to claim 5, wherein the polypeptide binds Flt4 and promotes proliferation of lymphatic endothelial cells that express Flt4.

10. A method according to claim 5, wherein the polypeptide binds the extracellular domain of Flt4 and stimulates Flt4 phosphorylation in mammalian cells expressing Flt4.

11. A method according to claim 5, wherein the polypeptide comprises a contiguous portion of SEQ ID NO: 8 that is sufficient to bind human Flt4EC,

wherein said contiguous portion includes eight cysteine residues that are conserved in human vascular endothelial growth factor (VEGF), human platelet derived growth factor A (PDGF-A), and human platelet derived growth factor B (PDGF-B), and

wherein said polypeptide lacks any portion of SEQ ID NO: 8 that has one or more cysteine motifs of a Balbiani ring 3 protein (BR3P).

12. A method according to claim 5, wherein the polypeptide comprises a portion of the amino acid sequence in SEQ ID NO: 8 effective to permit said binding to

the Flt4 extracellular domain, said polypeptide lacking at least carboxy-terminal residues of SEQ ID NO: 8 beyond residue 227.

Sub C3 13. A method according to claim 5, wherein the polypeptide is purifyable from conditioned media from a PC-3 prostatic adenocarcinoma cell line, said cell line having ATCC Accession Number CRL 1435, using an affinity purification procedure wherein the affinity purification matrix comprises a polypeptide comprising the extracellular domain of Flt4 receptor tyrosine kinase.

14. A method according to claim 5, wherein the polypeptide has an amino acid sequence consisting of a portion of the amino acid sequence set forth in SEQ ID NO: 8, said portion including from residue 161 of SEQ ID NO: 8 to residue 211 of SEQ ID NO: 8, said portion lacking at least carboxy-terminal residues of SEQ ID NO: 8 beyond residue 227.

15. A method according to claim 14, wherein the portion of the amino acid sequence set forth in SEQ ID NO: 8 includes from residue 131 of SEQ ID NO: 8 to residue 211 of SEQ ID NO: 8.

16. A method according to claim 14, wherein the portion of the amino acid sequence set forth in SEQ ID NO: 8 includes from residue 113 of SEQ ID NO: 8 to residue 213 of SEQ ID NO: 8.

17. A method according to claim 14, wherein the portion of the amino acid sequence set forth in SEQ ID NO: 8 includes amino acids 103 to 217 of SEQ ID NO: 8.

18. A method according to claim 14, wherein the portion of the amino acid sequence set forth in SEQ ID NO: 8 includes amino acids 32 to 227 of SEQ ID NO: 8.

Sub B3 19. A method of modulating the activity of Flt4 receptor tyrosine kinase (Flt4) in Flt4-expressing cells, comprising the steps of:

(a) preparing a polynucleotide comprising a nucleotide sequence that encodes a polypeptide that binds to the extracellular domain of human Flt4,

wherein said polynucleotide includes a strand that hybridizes to a DNA comprising the non-coding strand complementary to SEQ ID NO: 32, under the following hybridization conditions:

(i) hybridization at 42°C for 20 hours in a solution containing 50% formamide, 5x SSPE, 5x Denhardt's solution, 0.1% SDS and 0.1 mg/ml denatured salmon sperm DNA; and

(ii) washing the filter twice for thirty minutes at room temperature and twice for thirty minutes at 65°C with a wash solution containing 1x SSC, and 0.1% SDS;

(b) transforming or transfecting a cell with the polynucleotide such that the cell expresses and secretes a polypeptide encoded by said polynucleotide, wherein said secreted polypeptide binds the extracellular domain of human Flt4 and has a molecular weight of about 23 kD as assessed by SDS-PAGE under reducing conditions; and

(c) contacting Flt4-expressing cells with the secreted 23 kD polypeptide.

20. A method according to claim 19, wherein the polypeptide has an amino acid sequence comprising a continuous portion of the amino acid sequence shown in SEQ ID NO: 8 effective to permit said binding.

21. A method according to claim 19, wherein the polynucleotide comprises a nucleotide sequence that encodes the amino acid sequence shown in SEQ ID NO: 8, wherein the polynucleotide is transcribed and translated in the cell to produce a prepro-VEGF-C polypeptide having the amino acid sequence shown in SEQ ID No: 8, and wherein the prepro-VEGF-C polypeptide is proteolytically processed to form the 23 kD polypeptide.

22. A method according to claim 19, wherein the polynucleotide comprises the polypeptide-encoding insert of plasmid pFLT4-L, deposited as ATCC Accession No. 97231.

23. A method according to claim 19, wherein the polynucleotide further includes an expression control sequence operably linked to the sequence that encodes the polypeptide.

24. A method according to claim 19, wherein the transforming step comprises contacting the cell with vector that contains the polynucleotide.

25. A method according to claim 19, wherein the Flt4-expressing cells are human endothelial cells.

26. A method according to claim 25, wherein the human endothelial cells are lymphatic endothelial cells.

27. A method according to claim 25, wherein steps (b) and (c) are performed *in vivo*.

28. A method of modulating the proliferation of mammalian endothelial cells comprising the step of contacting mammalian endothelial cells with a composition comprising a polypeptide in an amount effective to modulate the proliferation of mammalian endothelial cells, said polypeptide comprising a VEGF-C ΔC_{156} polypeptide that binds to human Flt4 receptor tyrosine kinase (Flt4) and fails to bind to human KDR receptor tyrosine (VEGFR-2), said polypeptide having an amino acid sequence comprising a portion of SEQ ID NO: 8 effective to permit binding to Flt4, wherein the cysteine residue at position 156 of SEQ ID NO: 8 has been deleted or replaced by another amino acid.

29. A method according to claim 28, wherein the portion of SEQ ID NO: 8 is selected from the group consisting of:

(a) a continuous portion having as its amino terminal residue an amino acid between residues 102 and 114 of SEQ ID NO: 8 and having as its carboxy terminal residue an amino acid between residues 212 and 228 of SEQ ID NO: 8, wherein the

cysteine residue at position 156 of SEQ ID NO: 8 has been deleted or replaced by another amino acid;

(b) continuous portions that comprise an amino-terminal truncation of (a); and

(c) continuous portions that comprise a carboxyl-terminal truncation of (a) or (b).

30. A method according to claim 28, wherein said endothelial cells are lymphatic endothelial cells.

31. An *in vivo* method according to claim 28, wherein the contacting step comprises administering to a mammalian subject in need of modulation of the growth of lymphatic endothelial cells a composition comprising said polypeptide, in an amount effective to modulate the growth of lymphatic endothelial cells *in vivo*.

32. A method according to claim 31, wherein said polypeptide has reduced effect on the permeability of mammalian blood vessels compared to a wildtype VEGF-C polypeptide with an amino acid sequence set forth in SEQ ID NO: 8 from residue 103 to residue 227.

33. A method of modulating the proliferation of mammalian endothelial cells comprising the step of contacting mammalian endothelial cells with a composition comprising a polypeptide in an amount effective to modulate the proliferation of mammalian endothelial cells, said polypeptide comprising a fragment of a vertebrate prepro-VEGF-amino acid sequence that binds to human Flt4 receptor tyrosine kinase, with the proviso that, in said polypeptide, a conserved cysteine of the vertebrate prepro-VEGF-C has been deleted or replaced by another amino acid,

wherein the vertebrate prepro-VEGF-C amino acid sequence comprises an amino acid sequence that is encoded by a DNA of vertebrate origin which hybridizes to a

non-coding strand complementary to nucleotides 352 to 1611 of SEQ ID NO: 7 under the following hybridization conditions: hybridization at 42 C in a hybridization solution comprising 50% formamide, 5 X SSC, 20 mM $Na•PO_4$, pH 6.8; and washing in 0.2 X SSC at 55 C,

wherein nucleotides 352 to 1611 of SEQ ID NO: 7 encode a human prepro-VEGF-C having the amino acid sequence set forth in SEQ ID NO: 8 that is characterized by eight cysteine residues at positions 131, 156, 162, 165, 166, 173, 209, and 211 of SEQ ID NO: 8 that are conserved in human vascular endothelial growth factor (VEGF), human platelet derived growth factors A and B (PDGF-A, PDGF-B), human placenta growth factor (PlGF-1), and human vascular endothelial growth factor B (VEGF- B), and

wherein the conserved cysteine that has been deleted or replaced corresponds to position 156 of SEQ ID NO: 8.

34. A method according to claim 33, wherein the vertebrate is a human.

35. A method according to claim 33, wherein the vertebrate is a mouse.

36. A method according to claim 33, wherein said polypeptide comprises an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO: 8, wherein the cysteine residue at position 156 of SEQ ID NO: 8 has been deleted or replaced by another amino acid;

(b) the amino acid sequence of SEQ ID NO: 11, wherein the cysteine residue at position 152 of SEQ ID NO: 11 has been deleted or replaced by another amino acid;

(c) the amino acid sequence of SEQ ID NO: 13, wherein the cysteine residue at position 155 of SEQ ID NO: 13 has been deleted or replaced by another amino acid;

(d) amino-terminal truncations of (a), (b), or (c); and

(e) carboxyl-terminal truncations of (a), (b), (c), or (d).

37. An *in vivo* method according to claim 33, wherein the contacting step comprises administering to a mammalian subject in need of modulation of the growth of lymphatic endothelial cells a composition comprising said polypeptide, in an amount effective to modulate the growth of lymphatic endothelial cells *in vivo*.

38. A method for screening for inhibitors of the Flt4 receptor tyrosine kinase (Flt4), comprising the steps of:

contacting a cell that expresses Flt4 with a Flt4 ligand in the presence and absence of a putative inhibitor compound; and

assaying the Flt4 for autophosphorylation, wherein reduced autophosphorylation in the presence of the putative inhibitor compound versus the absence is identified as Flt4 inhibitory activity.

39. A method according to claim 38, wherein said Flt4 ligand is a polypeptide that:

(a) binds the extracellular domain of Flt4 receptor tyrosine kinase and stimulates Flt4 autophosphorylation;

(b) has an apparent molecular weight of about 23 kD as assessed by SDS-PAGE under reducing conditions; and

(c) has an amino acid sequence comprising a portion of SEQ ID NO: 8 effective to permit binding to the Flt4 extracellular domain.